DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Blvd.
Rockville MD 20850

DEC 4 2006

WARNING LETTER

Via Federal Express

Robert Ritch, MD
New York Eye and Ear Infirmary
310 East 14th Street
New York, NY 10003

Dear Dr. Ritch:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your clinical site from August 30 through September 11, 2006, by an investigator from the FDA New York District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical studies with the [redacted] sponsored by [redacted], complied with applicable federal regulations. The product used in the study is a device as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h). This letter also requests prompt corrective action to address the violations cited.

The FDA conducted the inspection under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions. At the close of the inspection, the FDA Investigator discussed observations made during the inspection. Our subsequent review of the inspection report is discussed below:

1. **Failure to conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by an IRB [21 CFR 812.110(b)].**

   Regarding the study titled: "[redacted]" under [redacted] you failed to adhere to the above-stated regulation. Examples of this failure include but are not limited to the following:

a.) The study protocol stated that "a [redacted]' was to be used in conjunction with the study device during the study procedure. However, you, and another physician who was participating in the study under your supervision, used a different [redacted] for at least 8 of the 16 subjects enrolled in the study. Specifically, you and Dr. Jeffrey Liebmann, your co-investigator, provided written confirmation to the FDA investigator that you used the [redacted] a [redacted] with different specifications, rather than the protocol-required [redacted] for the study procedure. You also stated that, in your opinion, the [redacted] and the [redacted] are "interchangeable."

As a clinical investigator, it is your responsibility to ensure that you and your study staff are familiar with the protocol and investigational plan, and that you are able to conduct the study in accordance with all protocol requirements. You also signed an investigator agreement in which you agreed to "properly perform and direct the Study in accordance with the Protocol."

b.) The IRB approval notification for this study, dated December 14, 2004, states that "no modifications may be made in the protocol…without prior approval of The New York Eye & Ear Infirmary IRB Committee." By using a [redacted] other than the one specified by the protocol, you failed to adhere to the conditions of approval imposed by the IRB. No record was found during the FDA inspection that this protocol modification was approved by the IRB prior to its implementation.

2. **Failure to obtain prior approval from the sponsor, the IRB, and FDA for deviations from the investigational plan that may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects [21 CFR 812.150(a)(4)].**

Regarding the Protocol [redacted] study, you failed to adhere to the above-stated regulation. Specifically, as detailed above, you and one of your co-investigators used a different [redacted] for at least 8 of the 16 subjects enrolled in the study. The investigator agreement you signed for this study also states that you will "immediately notify [redacted] and the relevant IRB/IRC of any failure to comply with or deviations from the Protocol." No records were found during the FDA inspection that this protocol deviation was approved by the sponsor, the IRB, or the FDA prior to its implementation.

3. **Failure to ensure FDA approval prior to allowing subjects to participate in a study [21 CFR 812.110(a)].**

Regarding the study titled: "[redacted]" you failed to adhere to the above-stated regulation. Specifically, you obtained IRB approval in October 2005 and subsequently enrolled 4 subjects in this study before the sponsor had requested or obtained approval for the study from the FDA. The sponsor subsequently suspended enrollment into this study by you in March 2006 when the sponsor discovered that you had prematurely begun recruiting subjects. In addition, records from the IRB indicated that this study was presented to the IRB as being conducted under [redacted] even though no such IDE exists for this study.

The violations described above are not intended to be an all-inclusive list of deficiencies that may exist at your clinical site. It is your responsibility as a clinical investigator to ensure compliance with the Act and applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. Failure to respond to this letter and take appropriate corrective action could result in FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 CFR 812.119.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the *FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators*, which can be found at http://www.fda.gov/oc/ohrt/irbs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Please send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Special Investigations Branch, (HFZ-311), 9200 Corporate, Rockville, Maryland 20850; Attention: Ms. Doreen Kezer, Branch Chief.

A copy of this letter has been sent to the FDA's New York District Office, Food and Drug Administration, 670 Federal Plaza, Room 670, Central Islip, NY 11722. We request that you copy the District Office on your response.

If you have any questions, please contact Ms. Doreen Kezer by phone at (240) 276-0125, or by email at doreen.kezer@fda.hhs.gov.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health